Grains Group
Concept to Commissioning

Marketing Potential For Generic Glyphosate In Canada

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Engineers & Planners

Table of Contents

1.0	Executive Summary	3
2.0	Objectives	9
3.0	Introduction	11
4.0	Patent Concerns	14
4.1	Discussion	14
4.2	Patent Abuse	15
4.3	Related Patents	17
4.4	Results of Patent Investigation	18
5.0	Market Potential	21
5.1	Existing Market	21
5.2	Potential For Increased Sales To Forest Industry	21
5.3	Potential For Increased Sales To Agriculture	22
5.4	Summary of Market Potential	26
5.5	Achievable Market Share	27
6.0	Regulatory Requirements	29
6.1	Pest Control Products Act	29
6.2	Food And Drug Act	29
6.3	Registration of Generic Glyphosate	30
6.4	Registration of New Uses For Glyphosate	32
6.5	Time And Costs of Registration	32
7.0	Product Manufacturing	34
7.1	Alternative One – Offshore Manufacturer	34
7.2	Alternative Two – Manufacturing In Canada	35
7.3	Preliminary Estimate Of Manufacturing Costs	35
7.4	Environmental Impact of Manufacturing Plant	37
7.5	Development of Manufacturing Technology	37
8.0	References	45
9.0	Appendix	46

1.0 Executive Summary

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Market Potential

Sales of glyphosate (as Roundup®) during 1987 were estimated to be approximately one and a half to two million litres per year. Agricultural uses accounted for 66 –75 % of all sales.

The future market potential for glyphosate will depend on three major factors; a) lower product cost , b) registration of new uses of glyphosate and c) the acceptance by farmers of herbicides as an alternative to mechanical tillage. The potential market for glyphosate is estimated to in the range of 4 – 5.5 million litres of formulated product per year. (Assuming a competitive formulated product cost). Of this estimated market demand, a new glyphosate herbicide product could be expected to capture approximately 25% of the total market, or from 1 – 1.4 million litres per year of formulated product.

Patent Concerns

Monsanto holds a patent covering the product glyphosate, the manufacture of glyphosate and the use of glyphosate as a herbicide. This patent will expire in 1990, after which generic glyphosate can be manufactured and sold in Canada using the method described in Canadian patent 936,865 without patent infringement. Monsanto has stated that they have no interest in issuing a license to allow the manufacture of glyphosate in Canada. It is anticipated that any challenge or attempt to circumvent the patent held by Monsanto will be both time consuming and expensive.

Regulatory Requirements

Generic glyphosate manufactured by any method for sale in Canada will require at least some form of supplemental registration under Agriculture Canada's policy of Product Specific Registration. The vague nature of the policy precludes an accurate definition of the time and cost that will be required to obtain registration. The best estimate available at this time is that registration will cost from $2 – $4 million dollars, and will take from one to two years to complete.

Product Manufacturing

Generic glyphosate has been offered by an offshore manufacturer (Pillar International Inc.) for approximately $12.00 per litre c.i.f. (cost, insurance, freight) Vancouver. The same company has expressed an interest in selling the manufacturing technology required to manufacture glyphosate in Canada. It is likely that competition from other offshore suppliers will yield a lower product price.

A preliminary analysis indicated that glyphosate could be produced for between $5.90 and $7.60 per litre. (This cost includes raw materials, manufacturing, packaging and warehousing.) Sales, advertising, distribution, dealership and registration costs are expected to increase the final product cost to a range of between $9.45 and $12.85 per litre.

The manufacturing facilities required to produce glyphosate would be similar in nature to industrial chemical plants located near industrial centers in Canada. The chemicals used in the manufacturing process would require similar care in handling to products such as chlorine or sulphuric acid. (These chemicals are shipped by rail car through Winnipeg on a regular basis.)

General

There is at least some risk that Monsanto will bring charges of patent infringement against anyone attempting to gain product specific registration prior to the expiration of Canadian patent number 936,865 on November 13, 1990.

Development of a new glyphosate production facility is considered to be the highest risk route to providing a marketable supply of generic glyphosate. It is anticipated that there will be considerable advertising and price competition from established herbicide manufacturers (including Monsanto) once the original patent expires. The cost and time required to obtain product specific registration will significantly increase the economic risks associated with this route.

The regulatory requirements that are currently in place have the effect of providing the original patent holder with an additional one to two years of protection from generic products.

The lowest risk route (from the legal and economic perspective) to providing a supply of glyphosate to the market will be to negotiate a supply contract with an offshore manufacturer. This contract should be negotiated prior to the expiration of Canadian patent number 936,865 (held by Monsanto), for implementation of product specific registration immediately following expiry of the patent.

A higher risk route (from a legal standpoint) for earlier initiation of the product registration procedures does exist whereby an application for a compulsory license would be made to the Commissioner of Patents on the grounds that glyphosate is not manufactured in Canada. While this application was pending the application for product specific registration would be made and any required field testing would be initiated. Until the patent held by Monsanto (936,865) expires, however, it would remain illegal to manufacture the product for commercial sale in Canada, and it is possible that use of the product for research leading to registration will also be ruled illegal.

The activity sheet shown in Diagram I illustrates the approach that should be taken to determine the potential for marketing glyphosate in Canada. This report represents Stage One of the program.

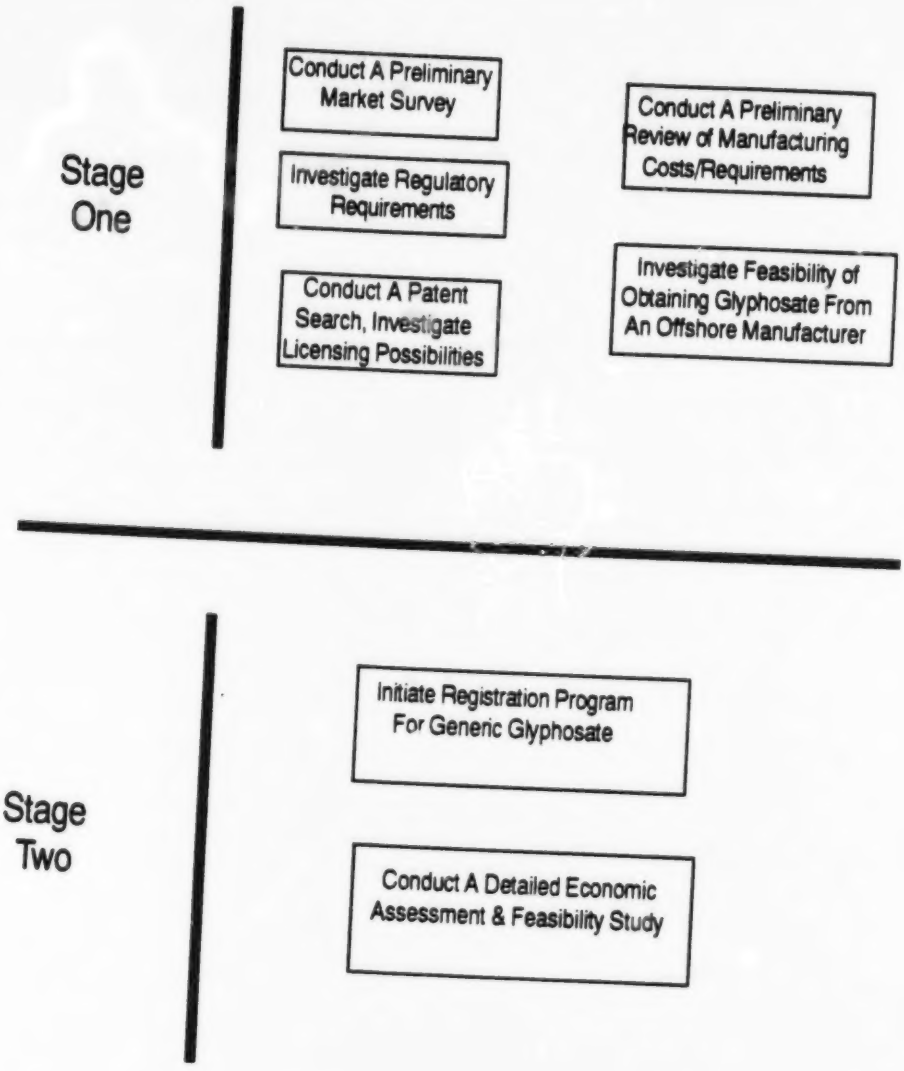
Stage One
Conduct A Preliminary Market Survey
Conduct A Preliminary Review of Manufacturing Costs/Requirements
Investigate Regulatory Requirements
Investigate Feasibility of Obtaining Glyphosate From An Offshore Manufacturer
Conduct A Patent Search, Investigate Licensing Possibilities
Stage Two
Initiate Registration Program For Generic Glyphosate
Conduct A Detailed Economic Assessment & Feasibility Study

Diagram 1

2.0 Objectives

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The objectives of this report are to provide specific information for the Government of Manitoba on the following topics:

- Present and future market potential for generic glyphosate
- The requirements for registration of new pesticides, with emphasis on generic herbicides such as glyphosate.
- The patents currently in effect that relate to either the manufacturing of glyphosate, the chemical glyphosate, or the use of glyphosate as a commercial product.
- The options available in acquiring a commercial scale supply of glyphosate for distribution and sale in Canada.

3.0 Introduction

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The herbicide glyphosate, commonly formulated under the trade name Roundup®, provides non-selective control of many annual and perennial weed species. It possesses unique properties such as low persistence, a wide range of herbicidal activity and low residual levels after contact with soil particles. It is a foliage applied type of herbicide, and acts by absorption through the foliage and translocation through the plant.

Non selective foliage control is of considerable value both to agricultural and industrial users. Glyphosate has a low level of toxicity to animals, birds and insects.[1,2] The product is easy to apply, with no unusual precautions required to protect personnel[2,3].

Soil degradation in Western Canada (due in large part to conventional tillage practices) has been identified as a major concern by the Senate Committee on Agriculture and Forests[4]. Losses due to soil degradation have been estimated to cost from $239 million to $1.3 billion annually by the Science Council of Canada[4]. Zero and reduced tillage cropping systems have shown considerable potential in some parts of Manitoba and the other prairie provinces in reducing this loss.

Glyphosate appears to have considerable economic and agronomic potential in Canada. This report identifies this potential, as well as the major factors relevant to it's manufacture and use.

4.0 Patent Concerns

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4.1 Discussion

A patent may cover any new useful "art, process, machine, manufacture or composition of matter" or any new and useful improvement to any of these things. For the purposes of this report, a patent may be directed towards any of the following items:

1. Glyphosate
2. Intermediate products in the production of glyphosate
3. Starting materials for the production of glyphosate
4. Methods of manufacturing any of the above.
5. Apparatus for manufacturing any of the above.

A patent search was conducted to locate all patents using "glyphosate" or the chemical equivalent "N-phosphonomethyl glycine".

The term of a Canadian patent is seventeen years from its date of issue, unless before that date the patent is the subject of a disclaimer or an adverse judgement affecting its validity in the courts. The patent term can only be extended by an act of Parliament.

The question of whether experimental manufacture and testing of a patented invention without the patentee's authorization is a patent infringement is not settled in Canada. The most relevant court decision seems to be that in Micro - Chemicals Limited et al v. Smith, Klyne and French Corp., (1971) 2 C.P.R. (2d) 193 where an applicant for a compulsory license had experimented with the

manufacture of a patented pharmaceutical before the compulsory license was granted. In deciding the case, the Supreme Court of Canada found that the experimental use in question was not an infringement of patent. The reasons given for so deciding are based at least to some extent on the existence of an application for a compulsory license under the relevant pharmaceutical provisions of the Patent Act. The court did, however, refer to the non-compulsory licensing case of Frearson v. Loe, (1878), 9 Ch. D. 48 which found that manufacture by way of bona fide experiments, without the intention of selling and making use of the product so made is not an infringement of a patent for the product manufactured. This was a British case however, and it is not clear that the precedent is fully applicable in Canada. The contrary argument is that unauthorized manufacture or use has placed the experimentor in a competitive position sooner than would have been the case had he acted properly and waited for the patent to expire. The patentee is thus injured by the unauthorized acts of the experimentor and may seek redress most likely in the form of an injunction before the expiry of the patent or damages after its expiry. This argument is analogous to the "springboard" principle in cases involving the misuse of confidential information. It is anticipated that a patentee, interested in maintaining an exclusive position with respect to the patented product for as long as possible, would seriously consider bringing action on this basis.

4.2 Patent Abuse

A patent provides an exclusive right to manufacture, use or to sell the invention. This exclusive right is subject to the compulsory licensing provisions of the Patent Act.

Apart from the compulsory licensing provision dealing specifically with food and medicine, any Canadian patent is subject to compulsory licensing where the patent right has been "abused". For the purposes of this report, the relevant abuses are:

1. Failure to work the invention within Canada on a commercial scale after three years from the date of issuing the patent. The Patent Act defines "work on a commercial scale" as "the manufacture of the article or the carrying on of the process described and claimed in a specification for a patent, in or by means of a definite and substantial establishment or organization and on a scale that is adequate and reasonable under the circumstances."

2. Preventing working of the invention on a commercial scale in Canada by importation from abroad.

3. Refusal to grant a license on reasonable terms, with consequent prejudice to the trade or industry of Canada, the trade of any person or class of persons trading in Canada or the establishment of any new trade or industry in Canada.

Section 67 of the Patent Act provides for the Commissioner of Patents to grant a compulsory license if the patent holder abuses his patent right.

Monsanto's main patent (Canadian patent No. 936,865) claims glyphosate compounds, phytotoxic compositions containing the compounds and the use of the compounds and compositions for vegetation control. The patent was issued on November 13, 1973. there is no manufacture of the product in Canada. Large quantities of imported product are sold and used for vegetation control in Canada. This means that it is open to any interested party to seek a compulsory license to manufacture, use and sell the product in Canada. Any application for compulsory license can be resisted by the patentee. Where the application alleges abuse by failure to work the invention in Canada, it is open to the patentee to argue that the time elapsed form the grant of the patent has been insufficient to enable working the invention in Canada on a commercial scale. Considerations such as lengthy regulatory approval procedures could be raised as appropriate reasons for non–working. It appears that in the case of glyphosates, the time elapsed has been sufficient to enable working in Canada.

4.3 Related Patents

Patent searches were conducted for patents relating to glyphosates, which are chemically described as :

N – phosphonomethyl glycines

This search revealed some 229 "families" of patents. Each "family" concerns a particular invention, say a particular process for manufacturing glyphosates, and contains the various published patents and patent applications directed to that invention. (Abstract listings for 145 of the patent families has been included in Appendix I). The patent search results were reviewed with a view to determining a cost effective method of producing glyphosate. Full copies of six patents that appeared promising and copies of other related patents have been included in Appendix II.

Assuming that the chemical synthesis pathways stated proved out after detailed laboratory analysis, it may be possible to obtain a manufacturing license from the patent holder. In the event the patent holder is unwilling to grant a licensing agreement, it may be possible to obtain a compulsory license on application to the Commissioner of Patents. This step assumes, of course, that the patent holder is "abusing" the patent right, for example by not manufacturing the chemical in Canada. Proving abuse where the patentee was not Monsanto could be difficult, as the patentee could plead the existence of Monsanto's dominating patents as a reason for not manufacturing.

4.4 Results of Patent Investigation

A detailed review of the original Canadian patent number 936,865 issued to Monsanto Company indicated that it is enforceable in all respects until the date of it's expiry, on November 13, 1990. This patent claims glyphosate compounds, compositions including glyphosate as an active ingredient, and methods of using the compounds and compositions for plant control. Canadian patent number 964,075 (issued to Monsanto Company) relates to the use of glyphosates in non-lethal amounts as growth-rate regulators.

In addition, the following conclusions regarding related patents can be made:

Any manufacture and sale of glyphosate and any plant growth inhibiting use of it would apparently infringe Canadian patent number 936,865. The use of glyphosates as plant growth regulators would apparently infringe Canadian patent number 964,075.

There are numerous patented manufacturing processes for glyphosates. The use of any such process, if patented in Canada, would, on the face of it, be an infringement of the patent for that process. Thus, for example, the use of the process patented in Stauffer Chemical Company's Canadian patent 1,188,315 (equivalent to U.S. patent 4,439,373) would infringe the Stauffer process patent as well as Monsanto's Canadian patent 936,865.

A compulsory license for the manufacture of glyphosates could be sought where an abuse of the patent right exists. Where a

license was to be sought from a party other than Monsanto, the patentee could reasonably argue that the existence of Monsanto's dominating patent 936,865 was adequate reason for the patentee's failure to work the invention before the expiry of the Monsanto patent. It is to be expected that the Commissioner of Patents would accept this position and defer the application for a compulsory license at least until the Monsanto patent expires. This argument is not available to Monsanto, and an application for compulsory license to work the invention under any of the Monsanto process patents would be more likely to succeed, although the likelihood of success cannot be quantified.

The alternative is to use a process that has been patented in another country but not Canada. This would avoid the need to seek a compulsory license.

Addition discussion titled "Glyphosate Patent Considerations" has been included in Appendix III.

5.0 Market Potential

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5.1 Existing Market

Estimates of sales of glyphosate in 1986 range from one and a half to two million litres. Of this, approximately 500,000 litres were sold to the forest industry[6] with the remainder being sold to the agricultural sector. All sales of glyphosate occurred as the herbicide Roundup®. It should be noted that the actual sales figures of Roundup® are confidential. The figures used in this report represent estimates from industrial and government sources.

5.2 Potential For Increased Sales to The Forest Industry

Glyphosate is used in the forest industry as a growth control tool in reforestation areas. Forestry officials indicated that the purchase cost was not a major factor in determining whether or not to use glyphosate. In most cases factors such as application cost, selectivity and environmental safety were considered to be of greater importance. The amount of glyphosate used was found to vary widely from province to province[6]. This variance in use seemed to be due to the different opinions of forestry officials on the value of using herbicides in reforestation work. No basis was identified for projecting a change in the market for glyphosate in the forest industry. It is expected that the market demand will remain relatively stable at approximately 500,000 litres per year.

5.3 Potential For Increased Sales To Agriculture

Glyphosate has gained wide acceptance in the agricultural sector for it's ability to provide control of hardy perennial weeds such as Quackgrass, Sowthistle and Canada thistle. It would appear that this represents the major area of use to date. The future sales potential for glyphosate is expected in the following areas:

A) Continued use in perennial weed control programs.

B) Reduced tillage (chem-fallow or zero till) programs.

C) Registration of glyphosate for crop desiccation.

D) Development of economic crops resistant to glyphosate

A) Use In Perennial Weed Control

Glyphosate was used on approximately 1.5 million acres in 1986. This estimate is based on 1.5 million litres applied at an average application rate of one litre per acre.

Results of a weed survey conducted in 1978 and 1979[7] indicated that there were more than six million acres in the prairie provinces infested with quackgrass. The cost of glyphosate seems to have been the major deterrent in spraying more acres. It would seem that if cost was not a factor that there is a market for sales of six million litres (1 litres per acre x 6 million acres). However, once quackgrass control has been achieved, respraying will not be required unless reinfestation occurs. If it can be assumed that the rate of reinfestation is 33% per year, then the average yearly infestation will be two million acres. This will reduce the anticipated demand for glyphosate as a mechanism of perennial weed control

to approximately two million litres per year. This would imply that there is limited potential for an increase in sales of glyphosate as a mechanism of perennial weed control.

B) Reduced Tillage (Chem-Fallow) Programs

There are approximately eighty million acres of farm land under cultivation in Western Canada. Of this, approximately twenty million acres are summerfallowed every year with the remainder seeded to crop.[8]

Typically, two to six mechanical tillage operations are required (depending on soil type and weed growth) throughout the season for weed control in summerfallow. Herbicides have the potential to replace at least some of the tillage operations required. Discussions with agricultural sources indicated that chemical costs was one of the major factors limiting the practice of chemical weed control in summerfallow. Mechanical tillage costs vary widely, depending on equipment used and soil type. The costs associated with summerfallowing have been estimated as shown below in Table 1.[10]

YEARLY COSTS ASSOCIATED WITH SUMMERFALLOW ($ / ACRE)

TYPE	HIGH	LOW	AVERAGE
Variable Costs	$16.42	$12.92	$14.67
Fixed Costs	$23.57	$12.69	$18.13
Total Costs	$39.99	$25.61	$32.80

TABLE 1

Since the majority of farmers own or have committed to purchasing their tillage equipment, the fixed cost component of summerfallowing would not change if they were to switch to chemical weed control in summerfallow. This means that the cost of using chemicals for weed control must be equal to or less than the variable costs of mechanical tillage, or less than the average variable cost of $14.67 per acre per year.

Glyphosate will provide weed control equivalent to or better than one mechanical tillage operation at an application rate of 1/2 litre to 1 litre per acre per application. The number of applications required per year will vary depending on weed growth, however, on average three applications will be required per year, for a requirement of between 1 1/2 and 3 litres per year. In order to be cost competitive with mechanical tillage, glyphosate must cost the farmer between $4.89 and $9.78 per litre of formulated product.

Other factors must be considered when evaluating glyphosate as an alternative to mechanical tillage. The amount of glyphosate used will depend on the acceptance of chem-fallow as an alternative to summerfallow by farmers. Other herbicides are available that provide a similar range of weed control to glyphosate at a cost of $12.00 to $24.00 per acre per year. (Estimates of chemical costs and recommended application rates for alternate herbicides were obtained from suppliers.) Since other chemicals are available that are cost competitive with the variable portion of mechanical tillage, it would appear that there is some resistance on the part of

farmers to using herbicides as an alternative to mechanical fallow. An accurate assessment of the market for glyphosate in chem-fallow will require a detailed market study. For the purposes of this report it was assumed that 10% of mechanical tillage operations would be replaced with chem-fallow, or:

10% x 20 million acres = 2 million acres per year.

If glyphosate could capture 50% (or 1 million acres) of this market the estimated market demand will be:

1 million acres x (1 1/2 – 3 litres per acre) = 1 1/2 – 3 million litres

C) Use of Glyphosate for Crop Desiccation.

Crop desiccant chemicals are used as an alternative to mechanical swathing to allow earlier harvesting of crops. Black soil zones, typically located in areas having cooler, wetter harvest seasons will receive the greatest benefit from the use of a crop desiccant. They cover approximately thirty million acres of Western Canada. Typically 80% of this area is seeded to crop[8] (24 million acres).

Glyphosate has not been registered for use as a crop desiccant in Canada, however, it has received registration in some European countries. It would be premature to produce an estimate of the market for glyphosate as a desiccant until preliminary field trials were carried out to determine if chemical residues would prevent registration. It should be noted that other crop desiccants have experienced residue problems in some crops such as lentils.

If glyphosate was to receive registration as a crop desiccant it would also provide pre-harvest control of perennial weeds such as quackgrass. A detailed market survey will be required to accurately determine the market demand for glyphosate in this market sector, however, it is not unreasonable to expect demand to be at least equal to the chem-fallow sector, or 1 1/2 to 3 million litres per year.

D) Development of Economic Crops Resistant to Glyphosate.

Plant geneticists have recently succeeded in producing crops that are resistant to glyphosate. This has the potential of making available varieties of canola and other valuable crops that are resistant to glyphosate. Glyphosate could then be sprayed as a post emergent herbicide, virtually eliminating all weeds from the crop. Since this work is still in the preliminary stages, the market potential for this application has not been included in this report.

5.4 Summary of Market Potential

A summary of the anticipated market for glyphosate is shown in Table 2.

Summary of Anticipated Market Demand For Glyphosate

TYPE OF USE	LITRES
Forestry	500,000
Perennial Weed Control	2,000,000
Chem-fallow	1,500,000 – 3,000,000
Desiccation	Unknown
Glyphosate Resistant Crops	Unknown
TOTAL	4,000,000 – 5,500,000

TABLE 2

5.5 Achievable Market Share

A major consideration when introducing a new product into the marketplace is the percentage of the available market that can be captured by the new product. Factors that will affect the share of market that can be captured by a new glyphosate herbicide are:

- Competitive action from Monsanto (price cuts, aggressive advertising, established distribution network and sales force, established product name.)
- New competition from other new herbicides, based on glyphosate or new chemical formulations. (e.g. Touchdown®)
- Reluctance of dealers to carry the new product.
- Reluctance of farmers to accept a new product.
- Selection of product marketing system (generic product manufacturer only, specific product manufacturer and wholesale distributor, or product manufacturer, distributor and retail sales)
- Registration of new product uses.

An accurate determination of the market share that could be captured by a new glyphosate herbicide will require a detailed market study. For the purposes of this report a market share of 25% has been assumed, as shown in Table 3.

Summary of Anticipated Market For A New Glyphosate Herbicide

Type of Use	Total Market Volume (L)	% Market Achievable	Achievable Volume (L)
Forestry	500,000	25%	125,000
Perennial Weed Control	2,000,000	25%	500,000
Chem-fallow	1,500,000 – 3,000,000	25%	375,000 – 750,000
Desiccation	Unknown	N/A	—
Glyphosate Resistant Crops	Unknown	N/A	—
TOTAL	4,000,000 – 5,500,000		1,000,000 – 1,375,000

TABLE 3

6.0 Regulatory Requirements

6.0 Regulatory Requirements

The use of herbicides in Canada is regulated by the Federal government. The relevant legislative acts are:

- The Pest Control Products Act.
- The Food And Drug Act.

6.1 Pest Control Products Act

The Pest Control Products Act (enacted in 1972) provides Agriculture Canada with the authority to regulate any product containing a pesticide regardless of label claims. At the federal level the term "pest control product" is used instead of the more common term "pesticide". In this report the term "pesticide" is used throughout.

The Pest Control Products Act requires that all pesticides be registered prior to sale or importation in Canada. This includes generic products and active ingredients that are used to manufacture formulated products.

6.2 Food And Drug Act

Health and Welfare Canada establishes permissible levels for chemical residuals in food products under authority granted to them by the Food And Drug Act. Tolerances are established on the basis of the toxicology of the pesticide, residues determined to be in a food product and consumption patterns for the food product in question.

The use of glyphosate as a crop desiccant prior to harvest will require field testing to determine chemical residue levels, if any, in the harvested crop.

6.3 Registration of Generic Glyphosate

Roundup® is the only major herbicide formulation containing glyphosate as an active ingredient that is currently registered for use in Canada The other two minor formulation registrations use glyphosate manufactured by Monsanto. It should be emphasized that it is the formulation Roundup® that is registered, not glyphosate. New herbicide formulations using glyphosate must be registered under the Pest Control Act prior to their use in Canada. The actual procedure used in obtaining registration will depend on the source and method of manufacture. Copies of the forms and regulations referred to in the following sections have been included as a supplemental to this report.

A) Importation of Glyphosate From An Offshore Manufacturer

Either the offshore manufacturer or the Canadian distributor would file an Application for Registration form and a Product Specification form. A draft label and a chemistry package in accordance with Trade Memorandum T-1-238 would also be submitted. Agriculture Canada laboratory technicians would review the chemistry information and determine if the new source is chemically equivalent. If chemical equivalence is not accepted the registration will be refused and the applicant would have the right of appeal to a Review Board for a review of the decision. If

chemical equivalency is accepted Agriculture Canada will send a letter to Monsanto to request that Monsanto determine the "point value" of it's eligible scientific data. The Point Value System is explained in detail in Trade Memorandum T-1-249. It is a system developed by the Crop Protection Institute of Canada with input from the Canadian Manufacturers of Chemical Specialties to assign relative values to scientific data bases. Monsanto will then have 60 days to respond to this request. If they fail to respond no points will be considered. If Monsanto does respond Agriculture Canada will review Monsanto's assessment of the point value. Once the point value has been established, Agriculture Canada will determine the research required by the applicant to meet 75% of the total point value. The applicant must then provide additional research as directed by Agriculture Canada, equal in monetary value to 75% of the total point value, in order to obtain product registration.

B) Glyphosate Manufactured in Canada by a Method Different From Monsanto's Registered Method

The procedure for registration of glyphosate manufactured by different method will be substantially the same as above. The T-1-238 chemistry package must be submitted to prove chemical equivalency. The point system will operate the same once chemical equivalency is accepted. A full data package would be required if chemical equivalency is not proven.

C) Glyphosate Manufactured Under License From Monsanto

Registration of glyphosate produced using Monsanto's manufacturing technology would be the easiest means of proceeding. The applicant would complete the registration forms and indicate that the method of manufacture is licensed from Monsanto. A letter from Monsanto confirming the license would be required. It is important that applicants negotiating such a license obtain the rights to access the scientific data package supporting the original registration as well as the manufacturing technology.

6.4 Registration of New Uses For Glyphosate

In order to register new uses of glyphosate the applicant must first register technical glyphosate as outline in the preceding sections. In addition, the applicant must submit to Agriculture Canada a complete data package supporting registration of the new use. If food residues are a concern, residue data will have to be submitted to Health and Welfare Canada.

6.5 Time And Cost of Registration

The best estimate that can be obtained at this time is that the cost of registration of glyphosate will range from $2 million to $4 million dollars. This estimate was obtained from discussion with Agriculture Canada officials. The actual cost of the original data package submitted by Monsanto is confidential.

7.0 Product Manufacturing

7.0 Product Manufacturing

There are two main alternatives available to a new potential distributor of a generic herbicide such as glyphosate in Canada:

- Purchasing from an offshore manufacturer
- Manufacture generic glyphosate in Canada

7.1 Alternative One - Purchasing From An Offshore Manufacturer

The potential Canadian distributor could purchase generic glyphosate from an offshore manufacturer. The product entering Canada must meet all pertinent regulations, be registered and must be legal for sale under existing patents. In this case the distributor will be concerned primarily with the distribution and sale of the product, rather than the development of the manufacturing technology and the subsequent production of the chemical product.

An example of an offshore company producing glyphosate is Pillar International Inc.[5]. The estimated cost to the distributor for the product will be approximately $11.50 - $12.50 (Can) per litre (as per quotation from Pillar International Co.[5])

Distribution, advertising and dealership costs are expected to be 30% of the product sales price, or $2.55 - $3.25 per litre. Registration costs would add from $1.00 to $2.00 per litre to the product cost. The product sale price will then range from $15.00 to $17.75 per litre.

7.2 Alternative Two - Manufacturing Generic Glyphosate In Canada

Constructing a new cost efficient, commercial scale plant will require the development of detailed manufacturing technology. This technology may be available by purchasing the technology from an offshore manufacturer such as Pillar International Inc. If this option is not considered viable, it will be necessary to develop the required technology "in-house". A logical process of developing this technology is outlined in Section 7.5 of this report.

7.3 Preliminary Estimate of Cost of Manufacturing Glyphosate

An estimate for commercial scale production costs of glyphosate was developed in the following manner:

a) Using a quotation from a generic supplier (Pillar International Inc..(5)).

Quoted Cost(c.i.f.) f.o.b. Vancouver — $12.16 Can

Assuming a "reasonable" mark-up of 50% yields a cost of manufacturing (including freight and packaging) of approximately $8.10 per litre.

If a freight and packaging cost of $1.00 per litre is assumed, the cost of manufacturing, including chemical costs would be approximately $7.10 per litre.

Note: The supplier indicated that this price was based on a one time order of one million litres. The price could be negotiated downward, depending on volume of order and length of supply contract established.

b) Using estimated chemical costs from patent information.

U.S. Patent No. 4,439,373

Chemicals Required:	Estimated Cost/kg
Glycine	$5.50 - $7.50
Sodium Carbonate	$0.20 - $0.30
Sodium Chloride	$0.30 - $0.40
37% aq Formaldehyde	$0.50 - $0.70
Phosphorous Acid	$6.00 - $6.80
Isopropylamine	$1.75 - $2.80

Using the yields indicated in the patent this produced a chemical cost of between $3.70 and $4.20 per litre of product. It should be emphasized that the chemical costs indicated above are preliminary estimates obtained by telephone quotes from various chemical suppliers. Large volume purchases and purchasing from specific suppliers of chemicals such as glycine could decrease chemical costs appreciably.

An accurate determination of the manufacturing costs will require a detailed analysis as outlined in section 7.5 of this report. For this report, manufacturing costs were estimated to range from 60 – 80% of raw chemical costs, or between $2.20 and $3.40 per litre of product. This would yield a product cost of between $5.90 and $7.60 at the plant warehouse.

Sales, advertising, distribution and dealership costs were estimated to be 30% of the sales price[4]. Registration costs would add from $1.00 to $2.00 per litre to the product cost. The cost of the product (before profit) to the customer would then be between $9.45 and $12.85 per litre.

7.4 Environmental Impact of Manufacturing Plant

The manufacturing procedures required to produce glyphosate are similar in characteristics to those used in many industrial plants located in Canada. The chemicals used as raw materials are typically transported across Canada by railcar on a regular basis. Waste emissions from the plant will not require any unusual treatment procedures. It should be noted that this estimate of environmental impact is based on a preliminary review of the chemical procedures required to produce glyphosate.

7.5 Development of Manufacturing Technology

The development program consists of three major phases:

- Phase I — Fundamental Research & Process Development
- Phase II — Process Demonstration & Market Planning
- Phase III — Commercial Plant Design & Construction

Each of these phases will involve a number of simultaneous and sequential activities geared to defining the technical and economic feasibility of producing generic glyphosate. At this stage it is assumed that the patent review and regulatory requirements studies will have indicated that it is feasible for the development program to proceed. As well, the preliminary market study will have determined the anticipated market volumes at different pricing structures.

- Phase I — Fundamental Research & Process Development

The first objective of this phase is to accomplish the basic

research and testing required to define a preliminary production process at the laboratory level. When dealing with the production of a generic product, at least some of the chemical synthesis information will be available from the patent information. The time and financial commitment required for this phase will depend to some degree on the results of the patent search and the review of regulatory requirements. If, for example, it is possible to use the original chemical synthesis process, then the amount of fundamental research required will be small, as will time and financial requirements. At the other extreme, if new chemical synthesis pathways are required, the amount of research required will be quite extensive. Some development at this level has already taken place at Atomic Energy of Canada (Pinawa) and POS Pilot Plant Corporation (Saskatoon).

Because of the patent and legal implications involved, all work should be carefully documented, with dates and witnesses listed in laboratory notebooks.

It is important that the final goal of the project, commercial production, be kept in mind during this phase. This means that preliminary process work should be developed around unit operations and techniques that can be translated into a commercial scale of operation. The key variables and areas that are critical to the process should be identified in detail. During the study the effect of using industrial grade chemicals and raw materials (rather than reagent grade) should be investigated. Laboratory reactors

should be operated over a wide range of conditions to simulate industrial conditions as closely as possible.

Of major concern will be the characteristics of the raw materials, the solvents used and the intermediate products. The consequences of a spill of any of the chemicals involved in the process should be carefully evaluated.

The second objective of this phase will be to develop the basis for a detailed economic feasibility – study. The economic feasibility study will be carried out in increasing detail throughout the three phases of the program. This study will be based on a commercial – scale facility, and will incorporate assumptions about the scaleability of the laboratory process. Scaleability can be defined as the process of translating the information obtained from the laboratory work into the detailed technical specifications required to build either a pilot plant or a full sized chemical production facility.

The greater the definition of the process that can be obtained in the laboratory, the more efficient will be the utilization of resources in either pilot plant research or commercial plant design.

The proposed size of the commercial plant should be determined as the first step of the feasibility analysis. This input normally comes from the market study. The proposed size of the plant will normally be determined by the projected growth of supply and demand, as well as the estimated level of production required when the product first enters the market.

The size-specific capital cost estimate can then be factored up

or down in scale to determine the sensitivity of manufacturing costs to changes in the size of the production facility. This procedure will help in determining the optimum size of the commercial facility.

After determining the size of the commercial facility, the remainder of the feasibility study can be carried out. A typical feasibility study will include the following major topics:

- Detailed process description
- Material & Energy Balances
- Process flow Diagrams
- Summary of Utility Requirements
- Detailed Equipment List
- A Description of Building Structure Requirements
- Special Process Requirements, Including:
  - Waste Product Treatment Requirements
  - Water Quality Requirements
  - Air Quality Requirements
  - Noise Abatement Requirements
  - Hazardous Goods Requirements.
  - Product Storage Requirements

A detailed cost estimate of equipment is generally not justified at this stage of the project. If the type of process to be used is reasonably well defined, a factored estimate will normally provide sufficient definition. The factored estimate can be obtained from vendor quotes and common equipment pricing lists.

Next, the installed cost of the facility is estimated. The feasibility study will:

- Summarize the capital cost estimates
- Provide a sensitivity analysis of operating costs
- Summarize technical assumptions
- Identify critical areas
- Provide a tentative construction schedule
- Include a cost estimate for pilot plant research

•Phase II — Process Demonstration & Market Planning

This phase has three major objectives:

- Demonstrate that the process is viable on a commercial scale.
- Obtain all necessary scale-up information
- Initiate the process of designing the commercial facility.

Questions regarding scaleability of equipment type, recovery yields, control of waste products and reaction times are usually resolved using pilot plant facilities. All remaining technical concerns must be resolved at this stage, and all technical, financial, business and legal concerns must be carefully coordinated.

During the pilot plant study the process is examined in much greater detail, which results in a better understanding of the different relationships of the process. Some questions that cannot be resolved in the laboratory will need to be resolved in the pilot plant. These are typically scale-up questions relating to reaction time, yield, reaction temperatures, etc. This information can then

be used to improve the accuracy of the process scale-up.

Those steps that can be scaled up by proven engineering principles do not need to be included in the pilot plant study, unless the steps are considered to be critical to the process.

The pilot plant will also supply product material for field trials and formulation studies. It is important that the product be tested as rapidly as possible, and that all regulatory requirements are met.

There are several options available for performing pilot plant work:

- Construction of a new pilot plant
- Utilizing existing pilot plant facilities

The design and construction of new pilot plant facilities will have the greatest impact on financial resources and on the overall project schedule.

For a new company, utilizing existing facilities on a contract basis can be quite attractive. Examples of Canadian facilities are; POS Pilot Plant Corporation (Saskatoon, Saskatchewan), and Atomic Energy of Canada (Pinawa plant site).

All planning for the commercial facility that has not been initiated should be started during this phase of the project. A site study should be started if no site has been selected. A definitive design and cost estimate should be prepared from the information obtained during the pilot plant study. Optimization of the process should be carried out to the greatest extent possible during the

pilot plant study.

•Phase III — Commercial Plant Design & Construction

The activities that make up this phase will include:

- Completion of definitive design & cost estimates
- Finalization of the financing plan & construction schedule
- Front-end engineering
- Obtaining environmental permits
- Equipment procurement
- Building construction & equipment installation
- Certification & startup

The design and construction of the commercial plant will bring together information from market surveys, economy of scale studies, pilot plant studies, site studies, and any other information that may reflect on the design of the plant.

At this stage of the project the chemical process is well understood, and the economics of a commercial scale facility have been well defined. Typically, the average chemical production facility will require 12 to 24 months from the beginning of the front-end engineering to actual startup of plant.

Front-end engineering involves the production of material and utility balances and final process flow diagrams. Detailed design work will involve the preparation of process and instrument diagrams, mechanical flow diagrams, equipment specifications and piping and instrument design.

After completion of the plant, the systems are checked, tested, started up and validated.

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Respectfully Submitted

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APPENDIX

APPENDIX I – Glyphosate Patent Considerations

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IN REPLY PLEASE REFER TO
OUR FILE NO.

Our File Ref: 48-3810

April 11, 1988

Mr. A. C. Roberts
UMA Engineering Ltd.
1479 Buffalo Place
Winnipeg, Manitoba
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Dear Mr. Roberts:

Re: Glyphosate Patent Considerations

We are writing pursuant to our discussions on April 6, 1988 at our office. We believe that the following will provide you with the information you require. We have attempted to deal with the various matters of interest under specific topic headings following a general discussion of the patent position with respect to glyphosates (including the two Canadian patents that you identified as the patents that required our review with respect to scope of protection being numbers 936,865 and 964,075).

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PATENT POSITION WITH RESPECT TO GLYPHOSATES

The dominant patent for glyphosates is Monsanto's Canadian patent 936,865. That patent issued on November 13, 1973. According to the Patent Office records it is in force as issued and will expire on November 13, 1990. The patent claims N-phosphonomethyl glycine compounds (in effect all glyphosates), compositions containing the compounds as an active phytotoxic ingredient, and methods of using the compounds and compositions for plant control.

Another patent of concern is Monsanto's Canadian patent 964,075 that issued on March 11, 1975. According to the Patent Office records, this patent remains in force as issued and will expire on March 11, 1992. The patent claims methods of regulating the natural growth or development of plants using certain glyphosates in non-lethal amounts.

There are numerous Canadian patents claiming various processes for producing glyphosates. These are granted to a number of different parties, including Monsanto Company.

Until the expiry of Canadian patent 936,865 on November 13, 1990, the only parties entitled to manufacture and sell glyphosates in Canada are:

(a) Monsanto Company;

(b) any party licensed to manufacture and sell glyphosates in Canada by Monsanto Company;

(c) the Government of Canada, including its agents and servants, subject to reasonable compensation paid to Monsanto Company.

Glyphosates may be used by any of the above parties and any of their customers.

The Government of Canada's right arises out of the Crown prerogative as limited by Section 19 of the Patent Act, which obliges the Government to pay the patentee a reasonable compensation for the use of the invention. This ability to use patented inventions extends to federal Crown corporations. This may be of importance as Atomic Energy of Canada Limited have, according to recently published reports, developed an ability to produce glyphosates. The production of glyphosates appears to be somewhat out of their normal range of activities however, and it may be necessary to investigate their standing to engage in such activities as an agent of the federal government.

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Provincial governments are not apparently bound specifically by the Patent Act, but most if not all of them have passed provincial statutes that have the effect of binding the respective provinces. In Manitoba the Proceedings Against The Crown Act, R.S.M. 1987, c. P140 provides that the Crown in right of Manitoba is liable for a tort committed by the Provincial Crown, its servants or agents. Patent infringement is considered a tort.

VOLUNTARY LICENSES

Monsanto have advised us verbally that they have no intention of licensing another party to manufacture and sell glyphosates in Canada.

COMPULSORY LICENSES

If the patents for glyphosates, their manufacturing processes and their use have been abused in any of the ways enumerated in Section 67 (2) of the Patent Act, an interested party may apply to the Commissioner of Patents for a compulsory license to be granted on terms set by the Commissioner of Patents. The enumerated abuses are:

> "(2) The exclusive rights under a patent shall be deemed to have been abused in any of the following circumstances:
>
> (a) If the patented invention (being one capable of being worked within Canada) is not being worked within Canada on a commercial scale, and no satisfactory reason can be given for such non-working, but if an application is presented to the Commissioner on this ground, and the Commissioner is of opinion that the time that has elapsed since the grant of the patent has by reason of the nature of the invention or for any other cause been insufficient to enable the invention to be worked within Canada on a commercial scale, the Commissioner may make an order adjourning the application for such period as will in his opinion be sufficient for that purpose;
>
> (b) if the working of the invention within Canada on a commercial scale is being prevented or hindered by the importation from abroad of the patented article by the patentee or persons claiming under him, or by persons directly or indirectly purchasing from him, or by other persons against whom the patentee is not taking or has not taken any proceedings for infringement;

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(c) if the demand for the patented article in Canada is not being met to an adequate extent and on reasonable terms;

(d) if, by reason of the refusal of the patentee to grant a licence or licences upon reasonable terms, the trade or industry of Canada or the trade of any person or class of persons trading in Canada, or the establishment of any new trade or industry in Canada, is prejudiced, and it is in the public interest that a licence or licences should be granted;

(e) if any trade or industry in Canada, or any person or class of persons engaged therein, is unfairly prejudiced by the conditions attached by the patentee, whether before or after the passing of this Act, to the purchase, hire, licence, or use of the patented article, or to the using or working of the patented process;

(f) if it is shown that the existence of the patent, being a patent for an invention relating to a process involving the use of materials not protected by the patent or for an invention relating to a substance produced by such a process, has been utilized by the patentee so as unfairly to prejudice in Canada the manufacture, use or sale of any such materials."

As we understand, Monsanto is not manufacturing glyphosates in Canada but is meeting the Canadian demand with imported products.

Clauses (a) and (b) could be set out as abuses in any application for a compulsory licence under Monsanto's patents.

With respect to clause (c) it is our understanding that the demand for glyphosate in Canada is being met by Monsanto to an adequate extent. You have suggested that the terms of supply may not be reasonable, due to excessive price, but this would be difficult to prove. In any event, clause (c), on the face of it, requires both an inadequate supply and unreasonable terms of supply in order for the state of abuse to exist.

An abuse under clause (d) is arguable at best. A prejudice to Canadian trade or industry would be difficult to establish as would prejudice to the public interest. This is especially if the Monsanto prices are to be reduced substantially.

Clauses (e) and (f) are not applicable in this case.

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On the basis of information now available to us, there are grounds for submitting an application for a compulsory licence under any of the Monsanto glyphosate related patents that are more than three years old. The application would be based on abuse of the patents by non-working and by preventing or hindering working by importation. There is a prima facie case of abuse on these grounds, although the possibility of success cannot be determined prior to making such application.

We expect that Monsanto would, in response to any such application, file a counter-statement disputing the existence of abuse, objecting to the proposal for compulsory licencing and any if not all of the proposed terms of such a licence, and countering with a proposal for very high royalties, at least equivalent to their profits on glyphosate sales. In the event of an adverse Commissioner's decision, Monsanto would have the right to appeal to the Federal Court. It could be expected that a Commissioner's decision would be delivered within about six months, in the absence of unexpected delays. Any appeal of that decision would, of course, incur further and possibly much longer, delays. It is possible that the compulsory licence proceedings could be extended past the expiry date of the basic glyphosate patent 936,865.

There are numerous Canadian patents issued to parties other than Monsanto for processes for manufacturing glyphosates. Voluntary licences may be available for some of these processes. It is unlikely that any application for a compulsory licence of any of these other patents would succeed until some significant time after November 13, 1990, as the patentee could reasonably plead the existence of Monsanto's patent 936,865 as sufficient reason for non-working until that date. Other processes have been patented in foreign countries but not in Canada. For those particular processes, no license would be required.

IMPORTATION

The importation of glyphosates before November 13, 1990 will, on the face of it, be an infringement of Monsanto's patent 936,865. In addition, the importation of glyphosate manufactured according to a process that is patented in Canada

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will be an infringement of the Canadian process patent whether Monsanto's or the process patent of some other party. Thus, where any glyphosate is to be imported, it is important to know and to be able to establish to the satisfaction of a Court the process by which it was manufactured.

EXPERIMENTAL USE

There is a principle, stated in Frearson v.Loe, (1878), 9 Ch.D 48 that manufacturing a patented product solely for the purpose of experiment to see if the product could be improved or if an improved process for producing the product could be developed, is not an infringement of the patent. This decision was adopted and extended somewhat by the Supreme Court of Canada in Micro-Chemical Limited et al v. Smith, Klyne and French Corp., (1971) 2 C.P.R. (2d) 193 where an applicant for a compulsory licence had experimented with the manufacture of a patented pharmaceutical before the compulsory licence was granted. The Supreme Court of Canada found that the experimental use in question was not an infringement of the patent. The Court observed that there was an application in place for a compulsory licence under the pharmaceutical provisions of the Act. They noted that the exemption from infringement appeared to be a logical result of the right to apply for a compulsory licence. Reference may also be made to the case of Hoffmann-LaRoche Limited v. Frank W. Horner Limited (1970) 61 C.P.R. 193 where the Quebec Superior Court refused an application for an interlocutory injunction in somewhat similar circumstances, but where the allegedly infringing medicine had been imported rather than manufactured locally. Neither case is conclusive as both deal with pharmaceuticals. In addition, in both cases, the alleged infringer's case was supported by the existence of an application for a compulsory licence under the pharmaceutical licensing provisions, which he would almost inevitably receive.

It could reasonably be argued that the importation of glyphosate for purely experimental purposes, with no intention of commercial gain from the use of the product, but with the express intention of obtaining regulatory approval of the glyphosate is analogous to the situation in the Micro-Chemical Case. The right to import acquired on expiry of the glyphosate product patent can be equated with the right to import acquired on issue of a compulsory licence. The contrary argument is available however, and the patentee could be expected to bring an action to restrain importation and use of the product.

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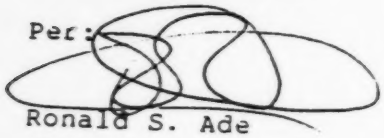
Attached for your consideration is a revised version of your report section 4.0 "Patent Concerns" which incorporates some of the foregoing information. Please let us know if we can do anything further.

Yours very truly,

FILLMORE & RILEY

Per: 

Ronald S. Ade

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